

## **AMENDMENTS TO THE SPECIFICATION:**

Please insert the following new paragraph, on page 1, line 1, of the specification:

## -- RELATED APPLICATION INFORMATION

This application is a 371 national stage entry of PCT/GB04/03512, filed August 16, 2004, which claims the benefit of priority from UK Application No. 0319167.3, filed on August 15, 2003. --

Please amend the paragraphs starting at page 3, line 9, and continuing through page 4, line 11, as follows:

Apolipoprotein C-III (hereinafter called Apo C-III). This is a candidate for the 11.7 kDa SELDI peak (as a glycosylated form). It has the Swiss-Prot accession number P02656, a length of 79aa, a molecular weight of 8765 Da and the following sequence:

GWVTDGESI KDYWSTVKDK FSEFWDI DPE VRPTSAVAA 99 (SEQ ID NO. 1)

Serum amyloid A protein (SAA). This is a candidate protein for the 11.5 and 11.7 kDa SAX2 SELDI peaks. It has the Swiss-Prot accession number P02735, a length of 103aa, a molecular weight of 11682 Da and the following sequence:

19 RS FFSFLGEAFD GARDMWRAYS DMREANYIGS DKYFHARGNY 60  
DAAKRGPGGV WAAEAISDAR ENIQRFFGHG AEDSLADQAA NEWGRSGKDP NHFRPAGLPE 120  
KY 122 (SEQ ID NO. 2)

Apolipoprotein C-1 (hereinafter called Apo C-1). This is a candidate protein for the 6.44 and 6.64 kDa SAX2 SELDI peaks. It has the Swiss-Prot accession number P02654, a length of 57aa, a molecular weight of 6631 Da and the following sequence:

27 TPDV SSALDKLKEF GNTLEDKARE LISRIKQSEL SAKMREWFSE TFQKVKEKLK IDS 83

(SEQ ID NO. 3)

Antithrombin III (Fragment). This is a candidate protein for the 4.47, 4.63 and 4.80 SAX2 SELDI peaks. It has the Swiss-Prot accession number P01008, a length of 38aa, a molecular weight of 4473 Da and the following sequence:

426 S LNPNRVTFKA NRPFLVFIRE VPLNTIIFMG RVANPCVK 464 (SEQ ID NO. 4)

Apolipoprotein A-1 (hereinafter called Apo A-I). This is a candidate protein for the 28 kDa SAX2 SELDI peak. It has the Swiss-Prot accession number P02647, a length of 244 aa, a molecular weight of 28079 Da and the following sequence:

DEPPQS PWDRVVKDLAT VYVDVLKDGS RDYVSQFEGS  
ALGKQLNLKL LDNWDSVTST FSKLREQLGP VTQEFDNLE KETEGLRQEM SKDLEEVKAK  
VQPYLDDFQK KWQEEMELYR QKVEPLRAEL QEGARQKLHE LQEKLSPNGE EMRDRARAHV  
DALRTHLAPY SDELRQRLLAA RLEALKENGG ARLAEYHAKA TEHLSTLSEK AKPALEDLRQ GLLPVLESFK  
VSFLSALEEY TKKLNTQ (SEQ ID NO. 5)

Please amend the paragraphs starting at page 14, line 8, and continuing through page 14, line 22, as follows:

Human Apolipoprotein LINCOplex Kit, (<http://www.lincoresearch.com/products/apo-62k.html>) Catalog # APO-62K is a multiplex assay kit manufactured by LINCO Research, Inc. and can be used for the simultaneous quantification of the following six apolipoproteins in any combinations: Apo AI, Apo AII, Apo B, Apo CII, Apo CIII, and Apo E. This kit can be used for the analysis of the above apolipoproteins in serum, plasma, tissue extract, other biological fluids, or tissue culture samples.

With regard to SAA determination, Dade Behring ([www.dadebehring.com](http://www.dadebehring.com)) provide in vitro diagnostic reagents for the quantitative determination of serum amyloid A (SAA) in human serum as well as heparinized and EDTA plasma by means of particle-enhanced Immunonephelometry using the BN Systems: N Latex SAA-Catalog OQMP11. A diagnostic kit is also commercially available from Dade Behring for the detection of ApoAI.

Please amend the paragraphs starting at page 21, line 21, and continuing through page 22, line 29, as follows:

## **EXAMPLE 7**

### **Protein identification by peptide fragmentation analysis (Q-TOF and MALDI-TOF/TOF)**

**Q-TOF:** Prior to nanoLC separation, the volumes of peptide containing solutions were adjusted to 7 $\mu$ l by addition of a 0.1% (v/v) formic acid solution. Samples were settled in a Triathlon autosampler (Spack, Emmen, Holland). For each experiment, 5 $\mu$ l of peptide containing solution were injected on a C18 reverse phase column of 75 $\mu$ m inner diameter (YMS-ODS-AQ200, Michrom Bioresource, Auburn, CA). Peptides were eluted with an acetonitrile gradient in the presence of 0.1% (v/v) formic acid, using SunFlow pumps (SunChrom, Friderichsdorf, Germany). A flow splitter was used in order to decrease the flow rate after the pumps from 200 to 0.4 $\mu$ l/min. Peptides were analysed with a Q-TOF mass spectrometer (Micromass, Wythenshawe, England). A 2700V tension was applied on the nano-electrospray capillary (New Objective, Woburn, MA, USA). Argon was used as collision gas. The collision energy was settled as a function of the precursor ion mass. MS/MS spectra were acquired by automatic switching between MS and MS/MS mode. Acquired MS/MS data were converted in a compatible format (DTA files) by ProteinLynx software (Micromass, Wythenshawe, England) and analysed using MASCOT search engine (<http://www.matrixscience.com>) with SWISS-PROT, TrEMBL, NCBInr and EST databases. In cases of manual interpretation of MS/MS data, identification was performed by sequence only search using ProteinInfo search engine from PROWL (<http://prowl.roekefeller.edu>).

**MALDI-TOF/TOF:** MS and MS/MS analyses were also performed on the Applied Biosystems Voyager TOF/TOF<sup>TM</sup> Workstation, which uses a 200Hz Nd:YAG laser operating at 355 nm. During

MS/MS analysis, air was used as the collision gas. Spectra were obtained by accumulation of 200 to 2000 consecutive laser shots. Peak harvesting was done automatically using Data Explorer software. Peak resolution was calculated using the Data Explorer software, with only baseline correction being applied to the raw data. The query was made for the bovine species with a minimum number of matched masses set as 4. The maximum tolerance for masses was 50 ppm after an internal calibration using autolysis products of trypsin, at most one missed cleavage for tryptic peptides was allowed, and the modifications accepted were carbamidomethyl cysteines and artifactual oxidation of methionines. SWISS-PROT & TrEMBL databases were used for the search. MS/MS interrogations were carried out, with the same parameters as previously described for the PMF research, using MS-TAG or MS-Pattern tools (<http://prospector.ucsf.edu/>) depending on the type of interrogation. Precursor peak error was set as 50-100 ppm and fragment tolerance was defined as 500-1500 ppm. No internal calibration of the MS/MS data was completed.